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(54) Pharmaceutical Composition for Prevention and Treatment of Periodontal Disease, Containing Titrated Extract of the Non-Saponifiable Fraction of *Zea Mays* and Magnolia Bark Extract

Abstract

This invention relates to a pharmaceutical composition that contains as active ingredients the titrated extract of the non-saponifiable fraction of *Zea mays* and magnolia bark extract, and is used for prevention and treatment of periodontal diseases.

The titrated extract of *Zea mays* non-saponifiable fraction has preventive and regenerative effects on alveolar bone resorption and periodontal ligament damage, and magnolia bark extract has significant bactericidal effect on anaerobic gram-negative bacteria and *Prevotella intermedia*, one of the pathogens involved in periodontal disease. The pharmaceutical composition containing the above two ingredients shows anti-inflammatory action and is far superior in efficacy in the prevention and treatment of periodontal diseases compared to other previously known periodontal disease drugs.

Key Words

Periodontal disease, magnolia bark extract, titrated extract of the non-saponifiable fraction of *Zea mays*, anti-inflammatory action, disinfectant action

Specification

Detailed Explanation of the Invention

Goal of the Invention

Field of Technology of the Invention and Prior Art

This invention relates to a composition for preventing and treating periodontal diseases and containing titrated extract of the non-saponifiable fraction of *Zea mays* and magnolia bark extract as active ingredients.

In periodontal disease, the loss of teeth clinically results from gingival bleeding and swelling, formation of periodontal pockets, destruction of alveolae, etc. Causes of periodontal disease include local factors and systemic factors, and in the event plaque as a local factor is mechanically accumulated within the periodontal pocket, it becomes a good habitat for the bacteria that exist around it, and this inhabitation gradually shifts from aerobic, air-permeable and gram-positive bacteria to anaerobic gram-negative

bacteria with proliferation at the deep portions of the periodontal pocket. Toxins and all products of proliferated anaerobic gram-negative bacteria directly damage tissue or stimulate the immune system to induce inflammation with periodontoclasia by a variety of actions on the part of the stimulated immune system.

As a defense mechanism against this, the function and immune reaction of polymorphonuclear leukocytes come into play as a systemic factor. However, antibacterial action and bacteriostatic action against the anaerobic gram-negative bacteria, elimination and destruction of toxic bacterial products, and regeneration of lost periodontal tissue are known to be crucial in the prevention and treatment of periodontal disease.

Since the 1920s, studies on the preventive agents and remedies for periodontal diseases have been performed. Particularly various countries in Europe and America have been focusing on plaque control using antibiotics and chemotherapeutic agents. These studies have been conducted more actively since 1970, when the pathogens responsible for periodontal disease were identified more clearly among the bacteria existing in the human body, and phenolic agents such as Listerine, quaternary ammonium compounds such as Scope, and chlorhexidine agents such as Peridex, have been launched on the market in Europe and America, and have been imported for sale on the Korean market as well.

The side effects of chemotherapeutic agents such as Listerine or Scope, are minor, but on the other hand, the anti-plaque and antibacterial effects of these agents are not remarkable. While Peridex, a chlorhexidine agent, is quite effective in its anti-plaque and antibacterial action, its adverse side effects are so critical that even its normal concentration of use, 0.12%, causes ulcerative stomatitis, desquamative gingivitis and pigmentation, etc, and adverse effects such as xerostomia in the case of long-term use. Consequently, there has been a need for agents with a regenerative action that simultaneously restore disrupted and lost periodontal tissue, exhibit antibacterial action and bacteriostatic action against anaerobic gram-negative bacteria, while eliminating inflammation, providing an ideal combination of preventive and therapeutic action against periodontal disease.

From this standpoint, while the inventor was conducting research on useful botanical products for prevention and treatment of periodontal disease, he developed the present invention based on his findings that magnolia bark extract is an agent that does not have the side effects such as microbial substitution, manifestation of bacterial resistance, desquamative exfoliation of periodontal tissue, and oncogenicity, in the case of long-term use, as exhibited by existing chlorhexidine antibiotics or antibacterial agents, ie, phenolic agents such as Listerine, quaternary ammonium compounds such as Scope, etc, yet selectively shows antibacterial action toward the pathogens in periodontal disease, for example, antibacterial action against *Streptococcus mutans*, a cariogenic bacterium (Japanese Patent Application Bulletin No. Se Pyeong 2-17524), and as reported (Korean Patent Application No. 92-16516) by the inventor, has excellent effects against *Prevotella intermedia,* a pathogen in periodontal disease, and is found to greatly reinforce the effect of titrated extract of the non-saponifiable fraction of *Zea mays* on the basis of experimental results obtained by mixing commercially available titrated extract of the non-saponifiable fraction of *Zea mays* and magnolia bark extract. The titrated extract of the non-saponifiable fraction of Zea Mays was reported to be effective in the prophylaxis and regeneration of alveolar bone absorption and the destruction of periodontal ligament when taken on a regular basis (Chaput, *L. Information Dentaire.* 1964, 23, 2148-2153). The agent was also reported to reduce looseness of teeth somewhat and to diminish the depth of paradental cysts (Ackerman et al, *L. Information Dentaire*, 1968, 8:751-758). In addition, it was reported that looseness of teeth decreased and the frequency of appearance of lamina dura was high after titrated extract of the non-saponifiable fraction of *Zea mays* was administered and modified Widman flap operations were performed (Choi, Deng, *Korean Academy of Periodontology Bulletin*, 1989, 19(1):63-70; *Korean Academy of Periodontology Bulletin* 1994, 24(3); 649-660).

These are commercialized products based on the above results and are currently on the market in many forms.

In the prior art, compositions using the magnolia bark extract for prevention and treatment of periodontal diseases have been published and described in several journals and patents, including Korean Granted Patent Publication No. 98-0176015 and No. 98-0143191, Korean Unexamined Patent Publication No. 96-0007923, and *Journal of Korean Academy of Periodontology*; vol. 22, No. 3, 1992; vol. 25, No. 3, 1995; vol. 26, No. 2, 1996; vol. 27, No. 1, 1997; and vol. 28, No. 4, 1998.

In the above-cited prior art studies, magnolol and honokiol extracted from magnolia bark were found to be safer than previously known antibacterial agents such as chlorhexidine, and were found to have a synergistic effect when used together with chlorhexidine, as well as significant bactericidal effect on *Prevotella intermedia* (Korean Unexamined Patent Publication No. 96-0007923). Further, when the magnolia bark extract, with its strong bactericidal effect on *Prevotella intermedia,* and *Gingko biloba* leaf extract, with its collagenase-suppressant and tissue-regenerative effects were used together, substantial anti-bacterial, bacteriostatic, anti-inflammatory, and tissue-regenerative effects were observed (Korean Granted Patent Publication No. 98-0143191). In addition, a composition made of *Zizyphi fructus* extract and the magnolia bark extract, the latter containing magnolol and honokiol as key ingredients, showed significant tissue-regenerative, anti-bacterial, and anti-inflammatory effects. In particular, this composition was found to be very effective in regenerating tissue because it eliminated the problem associated with the magnolia bark extract, ie, inhibition of periodontal tissue cell activity at high temperatures (Korean Granted Patent Publication No. 98-0176015).

The techniques mentioned above which use magnolia extract either solely or mixed with jujube extract and gingko leaf extract in specific proportions have the following positive effects on the prevention and treatment of periodontal diseases: (1) a significant restorative effect on weakened or damaged periodontal tissue, (2) suppression of inflammation reactions which destroy periodontal tissues, and (3) a strong anti-microbial effect against the pathogens of periodontal diseases without the adverse effects of conventional microbial agents. Magnolia extract is an effective anti-inflammatory and anti-microbial but may deactivate periodontal tissue cells when used in higher concentrations. Jujube extract and gingko leaf extract are also effective anti-inflammatory agents but not as effective as anti-microbial agents. In other words, they develop their action via fewer mechanisms to prevent and treat periodontal tissue.

Technical Goal of the Invention

This invention has been proposed on the basis of facts described above. In their experiment, the inventors mixed magnolia extract and non-saponified corn extract in an appropriate ratio, and found that adding magnolia extract highly enhanced the effectiveness of corn extract. The objective of this invention, therefore, is to provide a composition, which contains corn and magnolia extracts and is effective in the prevention and treatment of periodontal tissue disease.

Composition and Effects of the Invention

The corn extract used for this experiment was obtained in the following process: subject corn oil from corn germ to continuous primary saponification using caustic soda and organic solvent to produce extract that contains 40% non-saponified substance. This extract is then refluxed with alcoholic caustic soda extracts and concentrated by fluid extraction. Add alcohol to the resulting substance and filter it to collect sterol, and concentrate the filtered liquid to produce non-saponified extracts. For the magnolia extract, alcohol is added to magnolia from China or Japan, the resulting extract is filtered and concentrated. Only magnolia extracts containing over 1% of magnolol, one of the chief constituents, are chosen.

A conventional pharmaceutical delivery system may be added to the mixture of corn extract and magnolia extract, and various forms are available, such as pill, ointment, gargle liquid, and spray.

For instance, one may either include only the pure substance in a dental material or mix it with a conventional drug to manufacture an ointment or liquid to be used for the prevention and treatment of periodontal disease.

In addition, one may use the product orally after tooth brushing by adding it to a conventional gargle liquid, or spray it onto the area infected with a periodontal disease by preparing a mixture with a spray substance and introducing the mixture into a pressurized container. One may even benefit from a long-term preventive and therapeutic effect by using a toothpaste to which this substance is added for an extended period. In the production of these drugs, one may vary the mixing ratio of corn and magnolia extracts. Although the results vary slightly depending on the effectiveness of the topical agents and internal agents, the optimum weight ratio ranges between 0.5:1 and 1:1, yielding the best results. The mixture in the ratio ranging between 1.5:1 and 2.0:1 was somewhat less effective than that with a ratio of 0.5:1 and 1.0:1.

A detailed explanation of the invention will be given below using reference examples , experimental examples, and embodiments.

Reference Example 1: Production of Corn Extract

Corn extract was prepared as follows: 1 kg of corn oil extracted from corn germ was introduced into a round flask, and 10 L of *n*-nucleic acid was added to make a low viscosity liquid. 0.68 L of 5% caustic soda liquid was added, and the system was refluxed it for 3 hours at 55 C, then cooled for 2 hours at room temperature to separate the liquid into 2 layers. The fat and free fatty acid dissolved in the water were removed by saponification and neutralization. The remaining 0.045 kg of substance was dark brown and viscous and contained 40% non-saponified substance. This residue was transferred to a round flask for secondary saponification and the above procedure was repeated twice. The resulting substance was concentrated to obtain a dry material composed mainly of beta-phytosterol, a white crystal. A gas chromatographic analysis shows that it consists of about 70% beta-phytosterol, 6% campesterol, and about 16% alpha-phytosterol adding up to a total of 93% sterol, indicating that it is a relatively pure substance.

Reference Example 2: Production of Magnolia Extract

500 g *Magnolia officinalis* L. or Japanese magnolia (*M. obovata* Thunb.) is chopped and placed in a round flask and 3 L of 75% ethanol is added. Extraction is conducted for two hours in a 60 C water bath, and the system is cooled and filtered to obtain a filtrate. The same procedure is repeated on the residue to obtain a secondary filtrate, which is then added to the primary filtrate. The mixture is concentrated under vacuum to obtain an ethanol extract (90 g, 18%).

A quantitative analysis was done on this extract with HPLC using the chief component magnolol as the indicator. The material containing over 0.5% of this substance (Japanese Pharmacopoeia requires the content of magnolol to be over 0.8%) was chosen for the experiment.

Reference Example 3: Producing the Mixture of Corn Extract and Magnolia Extract

Corn extract and magnolia extract solutions in concentrations of 0.4% and 0.3%, respectively, are prepared and mixed in the weight ratios of corn extract : magnolia extract = 0.5:1, 1.0: 1, 1.5:1, and 2.0:1 for use in the experiment.

Experimental Example 1: Testing the Effects of the Mixture of Corn and Magnolia Extracts on the Activity of Gingival Fibroblasts

Gingival fibroblasts were collected from the premolar gingival area of orthodontic patients for culturing. Just prior to collection of the tissues, plaque and calculus were removed using a curette, and

irrigation was done several times with saline. An internal beveled incision was made in the interproximal area to excise the tissue. The collected tissue samples were cultured in α-minimal essential medium (α-MEM), containing 100 U/mL of penicillin, 100 μg/mL of streptomycin and 10% fetal bovine serum (FBS). The medium was replaced every three days and the cells cultured up to the fifth generation. To provide optimum culture conditions, the humidity and temperature were maintained at 95% and 37 C while 95% air and 5% CO_2 were continuously supplied. The daughter cells were mixed with 0.25% trypsin-EDTA and centrifuged to obtain the cell float, of which 1×10^6 cells were later introduced per well. In each well, 20 μL of the extract or extract mixture was added to 180 μL medium making a total of 200 μL. For optimized cultivating conditions, the humidity and temperature were maintained at 95% and 37 C while 95% air and 5% CO_2 were continuously supplied for 24 hours. After the culturing was completed, 50 μL of MTT (methyl thiazole-2-XL-2.5-diphenyl tetraolium bromide, Sigma Co., St. Louis, MO, USA) dissolved in saline was added to each well and kept in place for 4 hours. After removing MTT, 50 μl of DMSO was added to dissolve formazon crystals. After shaking the plate thoroughly, light absorbance was read at 570 nm using an enzyme linked immunosorbent assay (ELISA) reader (Thermo max, molecular devices, Menlo Park, CA, USA). As a control group for each experiment, α-MEM medium wells not containing the experimental solution were used. All results were expressed as percentages of the control group. As experiment substances, 0.4%, 0.3% corn extract, 0.4%, 0.3% magnolia extract and the mixture of the two in the respective ratios (0.5:1, 1:1, 1.5:1, 2:1) were used.

The experiment shows that corn extract and magnolia extract resulted in a significantly higher cell activity when mixed together in the ratio of 0.5:1 than when used singly. Even in the ratio of 1:1, mixed extracts resulted in a significantly higher cell activity than separate extracts. In the ratios of 1.5:1 and 2:1, mixed extracts still resulted in a cell activity that was lower than those in the ratios of 0.5:1, 1:1 but significantly higher than separate extracts. These results may be explained by a synergistic effect created between corn extract and magnolia extract (refer to Table 1).

[Table 1a]

Effects of extracts and their mixtures on the activity of gingival fibroblasts

Extract added		Cell activity (%)	Cell activity increase rate (each experiment group - control group)	Comparison of the increase in cell activity (%) (mixture/0.4%corn extract)
Control group (nothing added)		100		
0.4% corn extract		120.5	20.5	
0.4% magnolia extract		120.3	20.3	
Mixed substance of 0.4% corn extract (A) and 0.4%magnolia extract (B)	A:B=0.5:1	142.2	42.2	205.9%
	A:B=1.0:1	138.8	38.8	189.3%
	A:B=1.5:1	138.5	38.5	188.8%
	A:B=2.0:1	122.4	22.4	109.3%

* The same amount of substance (20 μL) (of either extract or mixture) was added in each well throughout the experiment.

* The increase rate of cell activity (%) was compared with the results of 0.4% corn extract addition.

[Table 1b]

The effects of extract and its mixtures on the activity of gingival fibroblasts

Extract added		Cell activity (%)	Cell activity increase rate (each experiment group - control group)	Comparison of increase in cell activity (%) (mixture/0.3% corn extract)
Control group (nothing added)		100		
0.3% corn extract		116.7	16.7	
0.3% magnolia extract		117.1	17.1	
Mixed substance of 0.3% corn extract (A) and 0.3% magnolia extract (B)	A:B=0.5:1	141.1	41.1	246.1%
	A:B=1.0:1	133.6	33.6	201.2%
	A:B=1.5:1	129.5	29.5	176.6%
	A:B=2.0:1	118.6	18.6	111.4%

* The same amount of substance (20 μL) (of either extract or mixture) was added in each well throughout the experiment.
* The increase rate of cell activity (%) was compared with the results of 0.3% corn extract addition.

Experimental Example 2 : Anti-Inflammatory Effects of the Mixture of Corn and Magnolia Extracts

1) Fibroblast Suppresses Interleukin-1β(IL-1β) Production

After counting the number of cells using a standard blood cell calculator, 5×10^5 cells were implanted in each well of a 24-well plate. The cells were cultured for 24 hours and the medium was then removed and washed with Hank's balanced salt solution (HBSS). Culturing was done once again for 24 hours with culture medium containing the respective extracts. The medium was then collected and washed with HBSS to be recollected. 0.02% EDTA-2.5% trypsin PBS (phosphate buffer solution) (10:1:9) was used to separate the cells, which were then centrifuged to remove the resultant upper layer. To collect IL-1β contained within, the cells were subjected to 3 freeze-thaw cycles and were then dissolved in 0.5 mL of phosphate buffer (pH=7.2, 13 mM phosphate. 0.15 M NaCl) and kept at 4 C for 30 minutes, then suspended. They were then centrifuged at 2000 × g for 10 minutes. Designated as Sample A, the upper layer fluid was used for quantitative analysis of interleukin-1β (IL-1β). The precipitate was sonified at 4 C for 2 minutes using a Branson sonifier cell disrupter B15 (Fisher USA) and floated in 0.5 mL of PBS. The resulting product was once again centrifuged and the resultant upper layer was gathered for IL-1β crystals (Sample B). The pellets were floated in PBS by a freeze-thaw cycle and then centrifuged. The resultant upper layer was collected for IL-1β crystals (Sample C). The total amount of IL-1β was obtained by adding up the amounts of IL-1β included in Samples A, B, and C. The concentration of IL-1β was measured with a highly sensitive interleukin-1β ELISA kit (Cistron Biotechnology, USA). Each extract and its mixture and non-specific binding (NSB) well were measured in duplicate in each ELISA well. 100 μL was added to each well and the NSB well was used as zero standard (matrix with no IL-1β). The wells were then covered and left at 37 C for 20 minutes. The wells were washed 3 times with wash buffer. 200-300 μL of buffer was added to each well, suspended for 30 seconds and aspirated. This washing process was repeated, and at the end of the last cycle the remaining wash buffer was removed with a clean paper

towel. 100 μL of IL-1β antiserum (rabbit) was added to each well and kept at 37 C for another 10 minutes. The wells were repeatedly washed using the method described above and 100 of μL anti-rabbit IgG-HRP conjugate was added to each well. The wells were covered, kept at room temperature for 20 minutes, washed using the same method, and 100 μL of IL-1β antiserum (rabbit) was added and the cells were cultured at room temperature for 10 minutes. 50 μL sulfuric acid was added and absorbance was measured at 450 nm using a microtitration plate reader (THERMO maxIM, Molecular Devices Co., USA) within 15 minutes.

In this experiment, IL-1β production was suppressed much more for both 0.4% and 0.3% corn extract solutions when corn extract and magnolia extract were mixed at a ratio of 0.5:1 instead of being used separately. It seems that mixing the two extracts created a synergistic effect. Such synergism was also observed when the two extracts were mixed in a ratio of 1:1. Those mixtures in the ratios of 1.5:1 and 2:1 were more effective for suppressing IL-1β production than corn extract functioning separately (refer to Table 2).

[Table 2a]

Effects of each extract and its mixture on suppressing the production of IL-1β

Extract added		Amount of IL-1β produced (pg)	Comparison of the suppression rate of IL-1β production (100-mixture/0.4% corn extract (%)
Control group		89	
0.4% corn extract		40	
0.4% magnolia extract		26	
0.4% corn extract (A) and 0.4% magnolia extract (B)	A:B=0.5:1	20	50%
	A:B=1.0:1	24	40%
	A:B=1.5:1	25	37.5%
	A:B=2.0:1	28	30%

* The control group was stimulated with lipopolysaccharide and no special medication was added
* The experiment group was stimulated with lipopolysaccharide and each experimental substance was added
* Lipopolysaccharide: a substance known to stimulate IL-1β production
* IL-1β: an inflammatory reaction mediator
* The same amount of substance (20 μL) (of either extract or mixture) was added in each well throughout the experiment.
* Pg: picogram
* The suppression rate of IL-1β production (%) was compared with the results of 0.4% corn extract addition.

[Table 2b]

Effects of each extract and its mixture on suppressing the production of IL-1β

Extract added		Amount of IL-1β produced (pg)	Comparison of the suppression rate of IL-1β production (100-mixture/0.3% corn extract (%)
Control group		89	
0.3% corn extract		44	
0.3% magnolia extract		28	
0.3% corn extract (A) and 0.3% magnolia extract (B)	A:B=0.5:1	24	45.5%
	A:B=1.0:1	26	40.9%
	A:B=1.5:1	29	34.1%
	A:B=2.0:1	31	29.5%

* The control group was stimulated with lipopolysaccharide and no special medication was added
* The experiment group was stimulated with lipopolysaccharide and each experimental substance was added
* Lipopolysaccharide: a substance known to stimulate IL-1β production
* IL-1β: an inflammatory reaction mediator
* The same amount of substance (20 μL) (of either extract or mixture) was added in each well throughout the experiment.
* Pg: picogram
* The suppression rate of IL-1β production (%) was compared with the results of 0.3% corn extract addition

2) Fibroblast Suppresses Prostaglandin E_2 (PGE_2) Production

Fifth- to seventh-generation gingival fibroblast cells were implanted in a 24-well plate (10^5 cells/well) with α-MEM and then divided. 1μg/mL of recombinant human interleukin -1β (rHu-1β, Genzyme, Co., Cambridge, MA, USA) was added to each well to stimulate prostaglandin E_2 (PGE_2) production. Each extract and its mixture were added to observe the effect in terms of suppressing PGE_2 production. Wells to which nothing was added constituted the control group. Each well was cultured in a sterile environment for 48 hours and then measured by a color comparison method using an ELISA reader with a PGE_2 enzyme immunoassay system (Amersham. In. Buckinghamshire, UK) at 450 nm.

In this experiment, PGE_2 production was suppressed much more for both 0.4% and 0.3% corn extract solutions when corn extract and magnolia extract were mixed at a ratio of 0.5:1 instead of being used separately. Mixing two extracts created a synergistic effect again. Suppression was observed in the mixtures in the ratios of 1:1, 1.5:1, and 2:1 (refer to Table 3).

The above two experiments verified the anti-inflammatory effect of the mixture of corn extract and magnolia extract and showed that the mixture is more effective than when corn extract is used separately. Much better anti-inflammatory effects were observed in the mixtures at ratios of 0.5:1 and 1.0:1.

[Table 3a]

Effects of each extract and its mixture on suppressing the production of PGE_2

Extract added		Amount of prostaglandin E_2 produced (pg)	Comparison of the suppression rate of prostaglandin E_2 production (100-mixture/0.4% corn extract (%)
Control group		62	
0.4% corn extract		16.5	
0.4% magnolia extract		8.6	
0.4% corn extract (A) and 0.4% magnolia extract (B)	A:B=0.5:1	6.8	58.8%
	A:B=1.0:1	7.8	52.7%
	A:B=1.5:1	7.6	53.9%
	A:B=2.0:1	8.6	47.9%

* The control group was stimulated with interleukin-1β and no special medication was added.
* The experiment group was stimulated with interleukin-1β and then each experimental substance was added.
* Interleukin -1β: a substance known to stimulate prostaglandin E_2 production
* Prostaglandin E_2: an inflammatory reaction mediator
* The same amount of substance (20 μl) (of either extract or mixture) was added in each well throughout the experiment.
* Pg: picogram
* The suppression rate of prostaglandin E_2 production (%) was compared with the results of 0.4% corn extract addition.

[Table 3b]

Effects of each extract and its mixture on suppressing the production of PGE_2

Extract added		Amount of prostaglandin E_2 produced (pg)	Comparison of the suppression rate of prostaglandin E_2 production (100-mixture/0.3% corn extract (%)
Control group		62	
0.3% corn extract		18	
0.3% magnolia extract		10.5	
0.3% corn extract (A) and 0.3% magnolia extract (B)	A:B=0.5:1	7.9	56.2%
	A:B=1.0:1	8.6	52.2%
	A:B=1.5:1	9.6	46.7%
	A:B=2.0:1	10.5	41.7%

* The control group was stimulated with interleukin -1β and no special medication was added.
* The experiment group was stimulated with interleukin-1β and then each experimental substance was added.
* Interleukin -1β: a substance known to stimulate prostaglandin E_2 production
* Prostaglandin E_2: an inflammatory reaction mediator
* The same amount of substance (20 μL) (of either extract or mixture) was added in each well throughout the experiment.
* Pg: picogram
* The suppression rate of prostaglandin E_2 production (%) was compared with the results of 0.3% corn extract addition.

The mixture of corn extract and magnolia extract from this invention may be manufactured with a conventional pharmaceutical delivery system such as pill, ointment, toothpaste, gargle liquid, and spray. The desirable mixing weight ratio of the two extracts (corn extract: magnolia extract) ranges between 1:0.5 and 1:2 (especially between 1:0.5 and 1:1). Some examples of compositions are listed below.

Examples of specific compositions and applications are given below for a more detailed explanation of this invention, which is by no means limited to these examples.

Embodiment 1: Phillip Coated Pill - 1 tablet (600 mg)

Corn extract	20 mg	
Magnolia extract		40 mg
Lactose		525 mg
Hydroxypropyl cellulose	5 mg	
Magnesium stearate	3 mg	
Glycerin		2 mg
Hydroxypropyl methylcellulose	5 mg	

Follow the conventional tablet manufacturing process. The dosage is three times a day, one pill each time

Embodiment 2: Phillip Coated Pill - 1 tablet (600 mg)

Corn extract	30 mg	
Magnolia extract		30 mg
Lactose		525 mg
Hydroxypropyl cellulose	5 mg	
Magnesium stearate	3 mg	
Glycerin		2 mg
Hydroxypropyl methylcellulose	5 mg	

Follow the conventional tablet manufacturing process. The dosage is three times a day, one pill each time.

Embodiment 3: Phillip Coated Pill - 1 tablet (600 mg)

Corn extract	40 mg	
Magnolia extract		20 mg
Lactose		525 mg
Hydroxypropyl cellulose	5 mg	
Magnesium stearate	3 mg	
Glycerin		2 mg
Hydroxypropyl methylcellulose	5 mg	

Follow the conventional tablet manufacturing process. The dosage is three times a day, one pill each time.

Embodiment 4: Ointment (the numbers indicate weight%)

Corn extract	0.20	
Magnolia extract		0.40
Carboxyvinyl polymer		7.00
Glycerol		30.00
Peppermint oil	0.006	
Propylene glycerol	30.00	
Add distilled water to make a total of 100 mL		

Mix the listed compositions to make an ointment, following the conventional ointment manufacturing process. Apply the ointment to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 5: Ointment (the numbers indicate weight%)

Corn extract	0.30	
Magnolia extract		0.30
Carboxyvinyl polymer		7.00
Glycerol		30.00
Peppermint oil	0.006	
Propylene glycerol	30.00	
Add distilled water to make a total of 100 mL		

Mix the listed compositions to make an ointment, following the conventional ointment manufacturing process. Apply the ointment to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 6: Ointment (the numbers indicate weight%)

Corn extract	0.40	
Magnolia extract		0.20
Carboxyvinyl polymer		7.00
Glycerol		30.00
Peppermint oil	0.006	
Propylene glycerol	30.00	
Add distilled water to make a total of 100 mL		

Mix the listed compositions to make an ointment, following the conventional ointment manufacturing process. Apply the ointment to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 7: Ointment (the numbers indicate weight%)

Corn extract	0.40	
Magnolia extract		0.80
Carboxyvinyl polymer		7.00
Glycerol		30.00
Peppermint oil	0.006	
Propylene glycerol	30.00	
Add distilled water to make a total of 100 mL		

Mix the listed compositions to make an ointment, following the conventional ointment manufacturing process. Apply the ointment to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 8: Ointment (the numbers indicate weight%)

Corn extract	0.60	
Magnolia extract		0.60
Carboxyvinyl polymer		7.00
Glycerol		30.00
Peppermint oil	0.006	
Propylene glycerol	30.00	
Add distilled water to make a total of 100 mL		

Mix the listed compositions to make an ointment, following the conventional ointment manufacturing process. Apply the ointment to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 9: Ointment (the numbers indicate weight%)

Corn extract	0.80	
Magnolia extract		0.40
Carboxyvinyl polymer		7.00
Glycerol		30.00
Peppermint oil	0.006	
Propylene glycerol	30.00	
Add distilled water to make a total of 100 mL		

Mix the listed compositions to make an ointment, following the conventional ointment manufacturing process. Apply the ointment to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 10: Spray (the numbers indicate weight%)

Corn extract	0.20	
Magnolia extract		0.40
Trichloromonofluoromethane	40.00	
Dichlorofluoromethane	44.85	
Peppermint oil	0.15	
Ethanol	6.00	
Polyethyleneglycol		8.40

Mix the listed compositions to make a spray filled in a compressed container, following the conventional spray manufacturing process. Apply the spray to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 11: Spray (the numbers indicate weight%)

Corn extract	0.30	
Magnolia extract		0.30
Trichloromonofluoromethane	40.00	
Dichlorofluoromethane	44.85	
Peppermint oil	0.15	
Ethanol	6.00	
Polyethyleneglycol		8.40

Mix the listed compositions to make a spray filled in a compressed container, following the conventional spray manufacturing process. Apply the spray to the area of periodontitis as needed to treat periodontitis and gingivitis.

Embodiment 12: Spray (the numbers indicate weight%)

Corn extract	0.40	
Magnolia extract		0.20
Trichloromonofluoromethane	40.00	
Dichlorofluoromethane	44.85	
Peppermint oil	0.15	
Ethanol	6.00	
Polyethyleneglycol		8.40

Mix the listed compositions to make a spray filled in a compressed container, following the conventional spray manufacturing process. Apply the spray to the area of periodontitis as needed to treat periodontitis and gingivitis.

Effectiveness of the Invention

As explained and illustrated through the embodiments above, the composition provided by this invention contains two effective elements that are combined to create a synergetic anti-inflammatory effect with which periodontal diseases can be effectively prevented and treated. One is corn extract, known to have a preventive and definite effect on alveolar bone and periodontal ligament destruction, and the other is magnolia extract, which is highly effective for sterilizing anaerobic gram-negative *Prevotella intermedia*, one of the pathogens in periodontal disease.

(57) Claims

1. Composition effective in preventing and treating periodontal diseases and characterized by corn extract and magnolia extract as its chief components, mixed in the weight ratio ranging between 0.5:1 and 2.0:1.

2. Composition effective in preventing and treating periodontal diseases in accordance with Claim 1, characterized by corn extract and magnolia extract mixed in the weight ratio ranging between 0.5:1 and 1.0:1.

3. Composition effective in preventing and treating periodontal diseases in accordance with Claim 1 or 2, characterized by the fact that its pharmaceutical form is selected from among tablet, ointment and spray.